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NEWS 5 AUG 13 Field Availability (/FA) field enhanced in BEILSTEIN  
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NEWS 7 AUG 18 Simultaneous left and right truncation added to PASCAL  
NEWS 8 AUG 18 FROSTI and KOSMET enhanced with Simultaneous Left and Right  
Truncation  
NEWS 9 AUG 18 Simultaneous left and right truncation added to ANABSTR  
NEWS 10 SEP 22 DIPPR file reloaded  
NEWS 11 SEP 25 INPADOC: Legal Status data to be reloaded  
NEWS 12 SEP 29 DISSABS now available on STN  
NEWS 13 OCT 10 PCTFULL: Two new display fields added  
NEWS 14 OCT 21 BIOSIS file reloaded and enhanced  
NEWS 15 OCT 28 BIOSIS file segment of TOXCENTER reloaded and enhanced  
  
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MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),  
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FILE 'HOME' ENTERED AT 19:09:17 ON 30 OCT 2003

=> index bioscience medicine

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.63	0.63

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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,  
BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,  
CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU,  
DGENE, DRUGB, DRUGLAUNCH, ...' ENTERED AT 19:10:57 ON 30 OCT 2003

# 71 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view search error messages that display as 0\* with SET DETAIL OFF.

=> s tag? (s) (vecto? or plasmi?) (s) cleav? (s) secret?

4 FILE AGRICOLA  
1 FILE BIOBUSINESS  
237 FILE BIOTECHABS  
237 FILE BIOTECHDS  
26 FILE BIOTECHNO  
4 FILE CABA  
8 FILE CANCERLIT  
2 FILE CAPLUS  
1 FILE CEABA-VTB

19 FILES SEARCHED...

1 FILE DISSABS  
38 FILE DGENE

25 FILES SEARCHED...

1 FILE DRUGU  
22 FILE EMBASE  
26 FILE ESBIODASE  
4\* FILE FEDRIP  
1 FILE FSTA  
10 FILE GENBANK

40 FILES SEARCHED...

34 FILE IFIPAT  
13 FILE LIFESCI  
7 FILE PASCAL  
1 FILE PROMT  
27 FILE SCISEARCH  
152 FILE USPATFULL

63 FILES SEARCHED...

2 FILE USPAT2  
15 FILE WPIDS  
15 FILE WPINDEX  
1 FILE NLDB

27 FILES HAVE ONE OR MORE ANSWERS, 71 FILES SEARCHED IN STNINDEX

L1 QUE TAG? (S) (VECTO? OR PLASMI?) (S) CLEAV? (S) SECRET?

=> d rankn

DISPLAY L# IS NOT VALID IN STNINDEX

Answer set was created in a file. Enter DISPLAY HISTORY to see where the answer set was created. Use the File command to change to that file, then display the answer.

=> d rank

F1 237 BIOTECHABS  
F2 237 BIOTECHDS  
F3 152 USPATFULL  
F4 38 DGENE  
F5 34 IFIPAT  
F6 27 SCISEARCH  
F7 26 BIOTECHNO  
F8 26 ESBIODASE  
F9 22 EMBASE  
F10 15 WPIDS  
F11 15 WPINDEX  
F12 13 LIFESCI  
F13 10 GENBANK  
F14 8 CANCERLIT  
F15 7 PASCAL  
F16 4 AGRICOLA

F17	4	CABA
F18	4*	FEDRIP
F19	2	CAPLUS
F20	2	USPAT2
F21	1	BIOBUSINESS
F22	1	CEABA-VTB
F23	1	DISSABS
F24	1	DRUGU
F25	1	FSTA
F26	1	PROMT
F27	1	NLDB

=> file f1-f10

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

2.75

3.38

FILE 'BIOTECHABS' ACCESS NOT AUTHORIZED

FILE 'BIOTECHDS' ENTERED AT 19:13:47 ON 30 OCT 2003

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FILE 'DGENE' ENTERED AT 19:13:47 ON 30 OCT 2003

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=> s tag? (s) (vecto? or plasmi?) (s) cleav? (s) secret?

7 FILES SEARCHED...

L2 577 TAG? (S) (VECTO? OR PLASMI?) (S) CLEAV? (S) SECRET?

=> dup rem

ENTER L# LIST OR (END):l2

DUPLICATE IS NOT AVAILABLE IN 'DGENE'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L2

L3 488 DUP REM L2 (89 DUPLICATES REMOVED)

<-----User Break----->

SEARCH ENDED BY USER

=> s l3 (s) histidin?

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L26 (S) HISTIDIN?'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L28 (S) HISTIDIN?'  
L4 62 L3 (S) HISTIDIN?

=> s l4 and enterokin?

L5 23 L4 AND ENTEROKIN?

=> s l5 and trypsi?

L6 12 L5 AND TRYPSI?

=> s l6 and (neuros? or kallikr?)

L7 10 L6 AND (NEUROS? OR KALLIKR?)

=> d ti l7 1-10

L7 ANSWER 1 OF 10 USPATFULL on STN

TI Novel human G-protein coupled receptor, HGPRBMY34, and variants and methods of use thereof

L7 ANSWER 2 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease EOS

L7 ANSWER 3 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease T

L7 ANSWER 4 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease C-E

L7 ANSWER 5 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease T

L7 ANSWER 6 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease EOS

L7 ANSWER 7 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease EOS

L7 ANSWER 8 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease T

L7 ANSWER 9 OF 10 USPATFULL on STN

TI DNA encoding the human serine protease EOS

L7 ANSWER 10 OF 10 USPATFULL on STN

TI DNA

=> d ibib abs l7 1-10

L7 ANSWER 1 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2003:219687 USPATFULL

TITLE: Novel human G-protein coupled receptor, HGPRBMY34, and variants and methods of use thereof

INVENTOR(S): Ramanathan, Chandra S., Wallingford, CT, UNITED STATES  
Gopal, Shuba, New York, NY, UNITED STATES  
Mintier, Gabriel A., Hightstown, NJ, UNITED STATES  
Feder, John N., Belle Mead, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003152977	A1	20030814
APPLICATION INFO.:	US 2002-314076	A1	20021206 (10)

NUMBER	DATE
-----	-----

PRIORITY INFORMATION: US 2001-338371P 20011206 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT  
DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000  
NUMBER OF CLAIMS: 20  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 14 Drawing Page(s)  
LINE COUNT: 8649

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes the novel human G-protein coupled  
receptor (GPCR) HGPRBMY34 and its encoding polynucleotide. Also  
described are expression vectors, host cells, antisense molecules, and  
antibodies associated with the HGPRBMY34 polynucleotide and/or  
polypeptide of this invention. In addition, methods for treating,  
diagnosing, preventing, and screening for disorders or diseases  
associated with abnormal biological activity of HGPRBMY34 are described,  
as are methods for screening for modulators, e.g., agonists or  
antagonists, of HGPRBMY34 activity and/or function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:310801 USPATFULL  
TITLE: DNA encoding the human serine protease EOS  
INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States  
Qi, Jenson, Branchburg, NJ, United States  
Andrade-Gordon, Patricia, Doylestown, PA, United States  
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United  
States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6485957	B1	20021126
APPLICATION INFO.:	US 1999-387375		19990831 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1999-303162, filed on 30 Apr 1999		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Wallen, III, John W.		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	12 Drawing Figure(s); 12 Drawing Page(s)		
LINE COUNT:	2185		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel  
serine protease we have termed protease EOS. The deduced amino acid  
sequence, and its alignment with other well-characterized serine  
proteases indicates that it is a member of the S1 serine protease  
family. We have found that the protease EOS mRNA is expressed in  
platelets and leukocytes and more specifically eosinophils. Although  
this protease is abundantly expressed in ovary, retina and stomach,  
where it may perform important functions, its expression in platelets  
and certain cells of the immune system suggests that it may play roles  
in thrombosis and in the immune process. Enzymatically active protease  
EOS is amenable to further biochemical analyses for the identification  
of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:301210 USPATFULL  
TITLE: DNA encoding the human serine protease T

INVENTOR(S) : Darrow, Andrew, Lansdale, PA, UNITED STATES  
Qi, Jenson, Branchburg, NJ, UNITED STATES  
Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002168754	A1	20021114
APPLICATION INFO.:	US 2002-41006	A1	20020107 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-386653, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Page(s)		
LINE COUNT:	2046		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T mRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dermatological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:294724 USPATFULL  
TITLE: DNA encoding the human serine protease C-E  
INVENTOR(S) : Darrow, Andrew, Lansdale, PA, UNITED STATES  
Qi, Jenson, Branchburg, NJ, UNITED STATES  
Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002164767	A1	20021107
APPLICATION INFO.:	US 2002-40803	A1	20020107 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-386629, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Page(s)		
LINE COUNT:	2065		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease C-E. The deduced amino acid sequence, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease C-E mRNA is expressed in pancreas, placenta, prostate, small intestine, stomach, spleen, fibroblasts and epidermis, as well as in certain regions of the brain

i.e., cerebellum, cerebral cortex, pituitary and hippocampus. Enzymatically active protease C-E, as produced using the methodologies described herein, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:265929 USPATFULL  
TITLE: DNA encoding the human serine protease T  
INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES  
Qi, Jenson, Branchburg, NJ, UNITED STATES  
Andrade-Grodon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002146805	A1	20021010
APPLICATION INFO.:	US 2002-40655	A1	20020107 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-386653, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Page(s)		
LINE COUNT:	2049		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T mRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dermatological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:258877 USPATFULL  
TITLE: DNA encoding the human serine protease EOS  
INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES  
Qi, Jenson, Branchburg, NJ, UNITED STATES  
Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142447	A1	20021003
APPLICATION INFO.:	US 2002-42091	A1	20020108 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		

NUMBER OF DRAWINGS: 17 Drawing Page(s)

LINE COUNT: 2153

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:258876 USPATFULL

TITLE: DNA encoding the human serine protease EOS

INVENTOR(S): Darrow, Andrew, Lansdale, PA, UNITED STATES

Qi, Jenson, Branchburg, NJ, UNITED STATES

Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142446	A1	20021003
APPLICATION INFO.:	US 2002-41264	A1	20020108 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	17 Drawing Page(s)		
LINE COUNT:	2167		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:254200 USPATFULL

TITLE: DNA encoding the human serine protease T

INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States

Qi, Jenson, Branchburg, NJ, United States

Andrade-Gordon, Patricia, Doylestown, PA, United States

PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION:	US 6458564	B1	20021001
APPLICATION INFO.:	US 1999-386653		19990831 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Wallen, III, John W.		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	2073		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease T. The deduced amino acid sequence encodes a prepro form of 290 amino acids, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease T mRNA is expressed in stomach, testis, retina, fibroblasts, spinal cord, and several regions of the brain. Protease T mRNA is also found in leukocytes and in the Jurkat (ATCC TIB-152) T cell line. Thus, this protease is potentially involved in gastric, testicular, retinal, dermatological, neurological/neurodegenerative and/or immunological disorders. The protease T gene maps to human chromosome 16p13.3 which is near the tryptase locus. Enzymatically active protease T, we have generated, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 10 USPATFULL on STN

ACCESSION NUMBER:	2002:206201	USPATFULL
TITLE:	DNA encoding the human serine protease EOS	
INVENTOR(S):	Darrow, Andrew, Lansdale, PA, UNITED STATES	
	Qi, Jenson, Branchburg, NJ, UNITED STATES	
	Andrade-Gordon, Patricia, Doylestown, PA, UNITED STATES	

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002110895	A1	20020815
APPLICATION INFO.:	US 2002-41400	A1	20020108 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-387375, filed on 31 Aug 1999, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003		
NUMBER OF CLAIMS:	27		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	9 Drawing Page(s)		
LINE COUNT:	2166		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease EOS. The deduced amino acid sequence, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease EOS mRNA is expressed in platelets and leukocytes and more specifically eosinophils. Although this protease is abundantly expressed in ovary, retina and stomach, where it may perform important functions, its expression in platelets and certain cells of the immune system suggests that it may play roles in thrombosis and in the immune process. Enzymatically active protease EOS is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 10 USPATFULL on STN

ACCESSION NUMBER: 2002:188232 USPATFULL

TITLE: DNA

INVENTOR(S): Darrow, Andrew, Lansdale, PA, United States  
Qi, Jenson, Branchburg, NJ, United States  
Andrade-Grodon, Patricia, Doylestown, PA, United States  
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6426199	B1	20020730
APPLICATION INFO.:	US 1999-386629		19990831 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Wallen III, John W.		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	2090		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Here we describe the molecular identification of a cDNA encoding a novel serine protease we have termed protease C-E. The deduced amino acid sequence, and its alignment with other well-characterized serine proteases indicates that it is a member of the S1 serine protease family. We have found that the protease C-E mRNA is expressed in pancreas, placenta, prostate, small intestine, stomach, spleen, fibroblasts and epidermis, as well as in certain regions of the brain i.e., cerebellum, cerebral cortex, pituitary and hippocampus. Enzymatically active protease C-E, as produced using the methodologies described herein, is amenable to further biochemical analyses for the identification of physiological substrates and specific modulators.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d kwic 17 1-10

L7 ANSWER 1 OF 10 USPATFULL on STN

DETD [0187] Host cells transformed with **vectors** containing nucleotide sequences encoding a HGPRBMY34 protein, or fragments thereof, may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be **secreted** or contained intracellularly depending on the sequence and/or the **vector** used. As will be understood by those having skill in the art, expression **vectors** containing polynucleotides which encode a HGPRBMY34 protein can be designed to contain signal sequences which direct **secretion** of the HGPRBMY34 protein through a prokaryotic or eukaryotic cell membrane. Other constructions can be used to join nucleic acid. . . facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as **histidine**-tryptophan modules that allow purification on immobilized metals; protein A domains that allow purification on immobilized immunoglobulin; and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of **cleavable** linker sequences such as those specific for Factor XA or **enterokinase** (Invitrogen, San Diego, Calif.) between the purification domain and the HGPRBMY34 protein may be used to facilitate purification. One such expression **vector** provides for expression of a fusion protein containing HGPRBMY34 and a

nucleic acid encoding 6 **histidine** residues preceding a thioredoxin or an **enterokinase cleavage site**. The **histidine** residues facilitate purification on IMAC (immobilized metal ion affinity chromatography) as described by J. Porath et al., 1992, Prot. Exp. Purif., 3:263-281, while the **enterokinase cleavage site** provides a means for purifying the 6 **histidine** residue **tag** from the fusion protein. For a discussion of suitable **vectors** for fusion protein production, see D. J. Kroll et al., 1993; DNA Cell Biol., 12:441-453.

DETD . . . herein or otherwise known in the art, such as, for example, the method set forth in Arakawa et al. (J. **Neurosci.** 10:3507-3515 (1990)); increased sprouting of neurons may be detected by methods known in the art, such as, for example, the methods set forth in Pestronk et al. (Exp. Neurol. 70:65-82 (1980)) or Brown et al. (Ann. Rev. **Neurosci.** 4:17-42 (1981)); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, etc., . . .

DETD . . . Examples of such immunogenic proteins include, but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean **trypsin** inhibitor. Various adjuvants may be used to increase the immunological response, depending on the host species, including but not limited. . . .

DETD . . . (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J. **Neurosurg.** 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., . . .

DETD . . . G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are **trypsinized** and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are **trypsinized** and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, . . .

L7 ANSWER 2 OF 10 USPATFULL on STN

SUMM Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification.

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage site** from human **trypsinogen I** (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac1 transplacement **plasmid** to generate PFEK-HA6XHIS-TAG FB.

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds

H.sub.20. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA.

- DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. *Gene* 41, 305-10.
- DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. *Biochemistry* 24, 8037-43.
- DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. *J. Biol. Chem.* 272, 21582-21588.
- DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. *Biol. Chem. Hoppe-Seyler* 376, 681-4.
- DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. *J. Biol. Chem.* 273, 11895-11901.
- DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. *Biochim. Biophys. Acta* 1350, 11-14.

L7 ANSWER 3 OF 10 USPATFULL on STN

- SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . . .
- DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.
- DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). *J. Biol. Chem.* 272:21582-21588) or physically. . . .
- DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). *J. Biol. Chem.* 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase** cleavage site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6XHIS affinity tag sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation vector described above has been cloned into a modified *Drosophila* expression plasmid to generate PFEK-6XHIS-TAG64.
- DETD . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole, followed by with a 1.5 ml wash with ds H.sub.20. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at. . . .
- DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. *Gene* 41, 305-10.
- DETD [0163] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. *Biochemistry* 24, 8037-43.
- DETD [0178] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997).

Characterization of the precursor of prostate-specific antigen  
Activation by **trypsin** and by human glandular  
**kallikrein**. J. Biol. Chem. 272, 21582-21588.

- DETD . . . . Z. -m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.
- DETD . . . . Ogawa, h., Takagi, K. -i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.
- DETD . . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 4 OF 10 USPATFULL on STN

- SUMM [0001] The members of the **trypsin**/chymotrypsin-like (S1) serine protease family are gaining recognition due to the increased awareness that these enzymes play pivotal roles in a multitude of diverse physiological processes. In addition to the classical functions the proteases **trypsin** and chymotrypsin perform during the digestive process, serine proteases also participate in regulating key amplification cascades through the proteolytic activation. . . .
- DETD . . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.
- DETD . . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . . .
- DETD . . . . (Miller et al. (1990). J. Clin. Invest. 86:864-700), Chymotrypsinogen SW:P17538 (Tomita et al. (1989). Biochem. Biophys. Res. Commun. 158:569-75), Glandular **Kallikrein** 1 SW:P06870 (Fukushima et al. (1985). Biochemistry 24:8037-43), **Trypsinogen** I SW:P07477 (Emi et al. (1986). Gene 41:305-10) and the translated rat BSP2 partial sequence GB:AJ005642 (Davies, et al. (1998) . . . .
- DETD . . . . in a manner similar to that previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase** cleavage site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac 1 transplacement **plasmid** to generate PFEK-6XHIS-TAG FB.
- DETD . . . . mM Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole], followed by a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the Ni-NTA agarose bead-bound PFEK-protease C-E-6XHIS zymogen in a 150. . . .
- DETD . . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.
- DETD [0167] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.
- DETD [0182] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen

Activation by **trypsin** and by human glandular kallikrein. J. Biol. Chem. 272, 21582-21588.

- DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.
- DETD [0189] Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.
- DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 5 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification. . . .

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase** cleavage site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6.times.HIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6.times.HIS affinity tag sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified Drosophila expression **plasmid** to generate PFEK-6.times.HIS-TAG64.

DETD . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole, followed by with a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at. . . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0165] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0180] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 6 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification.

DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG. The term "pro-sequence" as used herein refers to a nucleotide sequence that encodes a cleavage site for a . . .

DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically. . .

DETD . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage site** from human **trypsinogen I (EK)** fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine (6XHIS)** codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac1 transplacement **plasmid** to generate PFEK-HA6XHIS-TAG FB. The purified **plasmid** DNA of the full length protease EOS cDNA was used as a template in a 100 .quadrature.l preparative PCR reaction. . .

DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 .quadrature.g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA. . .

DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0129] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0152] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase cleavage site of trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin-like protease**. J. Biol. Chem. 273, 11895-11901.

DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin-like serine protease (neurosin)** preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 7 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse

physiological processes, including digestive processes and regulatory amplification.

DETD . . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically.

DETD . . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified pFastBac1 transplacement **plasmid** to generate PFEK-HA6XHIS-TAG FB.

DETD . . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 quadrature.g of zymogen) (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA.

DETD . . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD [0161] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned CDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD [0184] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD . . . . Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD . . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Acta 1350, 11-14.

L7 ANSWER 8 OF 10 USPATFULL on STN

SUMM Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification.

DETD . . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and



either inactivate (Takayama et al. (1997). J Biol. Chem. 272:21582-21588) or physically.

DETD . . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the 6XHIS affinity **tag** sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation **vector** described above has been cloned into a modified Drosophila expression **plasmid** to generate PFEK-6XHIS-TAG64.

DETD . . . . Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole, followed by with a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA beads in a 150 ul volume at.

DETD . . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.

DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.

DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.

DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.

DETD . . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.

DETD Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

L7 ANSWER 9 OF 10 USPATFULL on STN

SUMM [0001] Members of the **trypsin**/chymotrypsin-like (S1) serine protease family play pivotal roles in a multitude of diverse physiological processes, including digestive processes and regulatory amplification.

DETD . . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.

DETD . . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically.

DETD . . . . MoAb M2 anti-FLAG antibody epitope as previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase cleavage** site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding the hemagglutinin (HA) epitope and 6 **histidine** (6XHIS) codons for detection with the anti-HA antibody MoAb 12 CA5 (Boehringer Mannheim

Corp., Indianapolis, Ind.) and affinity purification on nickel resins respectively. A unique Xba I restriction enzyme site, immediately upstream of the epitope/affinity tag sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation vector described above has been cloned into a modified pFastBac1 transplacement plasmid to generate PFEK-HA6XHIS-TAG FB.

- DETD . . . 15 mM imidazole], followed by with a 1.5 ml wash with ds H.sub.2O. Zymogen cleavage was carried out by adding **enterokinase** (10 U per 50 .quadrature.g of zymogen) (Novagen, Inc., Madison, Wis.; or Sigma, St. Louis, Mo.) to the zymogen-bound Ni-NTA.
- DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.
- DETD [0166] Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.
- DETD [0189] Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.
- DETD . . . Z. -m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.
- DETD . . . Ogawa, h., Takagi, K. -i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.
- DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

#### L7 ANSWER 10 OF 10 USPATFULL on STN

- SUMM The members of the **trypsin**/chymotrypsin-like (S1) serine protease family are gaining recognition due to the increased awareness that these enzymes play pivotal roles in a multitude of diverse physiological processes. In addition to the classical functions the proteases **trypsin** and chymotrypsin perform during the digestive process, serine proteases also participate in regulating key amplification cascades through the proteolytic activation.
- DETD . . . and are suitable for use in the present invention. Examples of suitable pre-sequences include, but are not limited to, prolactinFLAG, **trypsinogen**, and chymoFLAG.
- DETD . . . conditions, which often require high protein concentrations. The second method is the use of a surrogate activating protease, such as **trypsin**, to cleave the serine protease under investigation, and either inactivate (Takayama et al. (1997). J. Biol. Chem. 272:21582-21588) or physically.
- DETD . . . (Miller et al. (1990). J. Clin. Invest. 86:864-700), Chymotrypsinogen SW:P17538 (Tomita et al. (1989). Biochem. Biophys. Res. Commun. 158:569-75), Glandular **Kallikrein** 1.SW:P06870 (Fukushima et al. (1985). Biochemistry 24:8037-43), **Trypsinogen** I SW:P07477 (Emi et al. (1986). Gene 41:305-10) and the translated rat BSP2 partial sequence GB:AJ005642 (Davies, et al. (1998).. . .
- DETD . . . in a manner similar to that previously described (Ishii et al. (1993). J. Biol. Chem. 268:9780-6) for the purposes of **secretion** and antibody detection respectively (PF). Significantly, this construct also contains the **enterokinase** cleavage site from human **trypsinogen** I (EK) fused in-frame and downstream from the signal sequence. At the C-terminus, preceding a stop codon, are additional sequences encoding 6 **histidine** (6XHIS) codons for affinity purification on nickel resins. A unique Xba I restriction

enzyme site, immediately upstream of the epitope/affinity tag sequence and downstream of the PFEK prepro sequence described above, and is the point of in-frame insertion of the catalytic domain of a heterologous serine protease cDNA (FIG. 4). The zymogen activation vector described above has been cloned into a modified pFastBac1 transplacement plasmid to generate PFEK-6XHIS-TAG FB.

- DETD . . . mM Tris-HCl (pH 8.0), 300 mM NaCl, and 15 mM imidazole], followed by a 1.5 ml wash with ds H.sub.2O. **Enterokinase** cleavage was carried out by adding **enterokinase** (Novagen, Inc., Madison Wis.; or Sigma, St. Louis, Mo.) to the Ni-NTA agarose bead-bound PFEK-protease C-E-6XHIS zymogen in a 150. . .
- DETD . . . T., Nishide, T., Mori, T., and Matsubara, K. (1986). Cloning, characterization and nucleotide sequences of two cDNAs encoding human pancreatic **trypsinogens**. Gene 41, 305-10.
- DETD Fukushima, D., Kitamura, N., and Nakanishi, S. (1985). Nucleotide sequence of cloned cDNA for human pancreatic **kallikrein**. Biochemistry 24, 8037-43.
- DETD Takayama, T. K., Fujikawa, K., and Davie, E. W. (1997). Characterization of the precursor of prostate-specific antigen Activation by **trypsin** and by human glandular **kallikrein**. J. Biol. Chem. 272, 21582-21588.
- DETD Wang, Z.-m., Rubin, H., and Schechter, N. M. (1995). Production of active recombinant human chymase from a construct containing the **enterokinase** cleavage site of **trypsinogen** in place of the native propeptide sequence. Biol. Chem. Hoppe-Seyler 376, 681-4.
- DETD . . . K.-i., Ogawa, h., Takagi, K.-i., Umemoto, N., and Yasuoka, S. (1998). Cloning and characterization of the cDNA for human airway **trypsin**-like protease. J. Biol. Chem. 273, 11895-11901.
- DETD . . . N., Kodama, S., Tsujimoto, M., Yamamura, Y., Tanaka, T., Nakazato, H., and Yamaguchi, N. (1997). Molecular cloning of a novel **trypsin**-like serine protease (**neurosin**) preferentially expressed in brain. Biochim. Biophys. Acta 1350, 11-14.

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(FILE 'HOME' ENTERED AT 19:09:17 ON 30 OCT 2003)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, ...' ENTERED AT 19:10:57 ON 30 OCT 2003

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1   FILE BIOBUSINESS
237 FILE BIOTECHABS
237 FILE BIOTECHDS
26  FILE BIOTECHNO
4   FILE CABA
8   FILE CANCERLIT
2   FILE CAPLUS
1   FILE CEABA-VTB
1   FILE DISSABS
38  FILE DGENE
1   FILE DRUGU
22  FILE EMBASE
26  FILE ESBIODASE
4*  FILE FEDRIP
1   FILE FSTA
10  FILE GENBANK
34  FILE IFIPAT
13  FILE LIFESCI

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7 FILE PASCAL  
 1 FILE PROMT  
 27 FILE SCISEARCH  
 152 FILE USPATFULL  
 2 FILE USPAT2  
 15 FILE WPIDS  
 15 FILE WPINDEX  
 1 FILE NLDB

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 L4 62 S L3 (S) HISTIDIN?  
 L5 23 S L4 AND ENTEROKIN?  
 L6 12 S L5 AND TRYPSI?  
 L7 10 S L6 AND (NEUROS? OR KALLIKR?)

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
32.81	36.19

FULL ESTIMATED COST

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